

### **Remarks**

Applicant appreciates the thorough examination of the present application as evidenced by the Office Action dated July 16, 2002 (the Action). Claims 22-50 are pending in the present application. Claims 25-29, 33-36, 38-43, 45-48 and 50 are withdrawn from consideration. Claims 22-24, 31-32, 37, 44, and 49 stand rejected under 35 U.S.C. § 103(a). Applicant has added new Claims 51-53. New Claims 51-53 are directed toward a preferred embodiment and are presented to complete the record. Support for new Claims 51-53 can be found in existing Claims 22-24, 31-32, 37, 44, and 49, among other places. The concerns raised by the Examiner are addressed below as set forth in the Action.

#### **I. Newly Added Claims**

Applicant has added new Claims 51-55. Support for new Claims 51-53 can be found in existing Claims 22-24, 31-32, 37, 44, and 49, among other places.

New Claims 51-53 are directed toward a preferred embodiment relating to a method of administering a sodium channel blocker to an airway surface of a subject in need thereof, comprising administering the sodium channel blocker in an effective therapeutic amount in a vehicle, said vehicle comprising potassium sulfate as an ionic osmolyte, said potassium sulfate included in an amount effective to increase the volume of liquid on the airway surface. The claims further clarify that in a particular embodiment, the subject is afflicted with cystic fibrosis. The claims further provide that in particular embodiments, the administering step is an aerosol inhalation administering step. The recitations of newly added Claims 51-53 are clearly not taught or suggested by the cited references, and thus, Applicant respectfully submits that new Claims 51-53 should be allowed.

#### **II. Rejection Under 35 U.S.C. § 103**

Claims 22-24, 31-32, 37, 44, and 49 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,817,028 to Anderson (Anderson), in view of U.S. Patent No. 5,876,700 to Boucher, Jr. et al. (Boucher, Jr. et al.) and U.S. Patent No. 5,837,266 to Jungherr et al. (Jungherr et al.). More specifically, the Action states that "it would have been prima facie obvious to a person of ordinary skill in the

art, at the time the claimed invention was made, to treat a subject with cystic fibrosis by administering to the subject a combination of osmolyte, such as potassium sulfate and a sodium channel blocker, such as benzamil or phenamil.” Action, page 3. Applicant respectfully traverses this rejection.

Applicant notes that under 35 U.S.C. § 103, references, when combined, must teach or suggest *all* the recitations of the claims, and there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. M.P.E.P. §2143. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. M.P.E.P. §2143.01, citing *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). The Court of Appeals for the Federal Circuit has further stated that, to support combining or modifying references, there must be particular evidence from the prior art as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. *In re Kotzab*, 55 U.S.P.Q.2d 1313, 1317 (Fed. Cir. 2000).

As further clarified in New Claim 51, an embodiment of the invention is directed to administering a sodium channel blocker to an airway surface of a subject in need thereof, comprising administering the sodium channel blocker in an effective therapeutic amount in a vehicle, said vehicle comprising potassium sulfate as an ionic osmolyte, said potassium sulfate included in an amount effective to increase the volume of liquid on the airway surface. In contrast, Anderson proposes the following:

“[A] method for attempting to provoke airway narrowing in a subject comprising the steps of (a) causing the subject to inhale into the airways an effective amount of a substance capable of altering the osmolarity of airway surface liquid in the subject, which substance is in the form of a dispersible dry powder containing an effective proportion of particles of a respirable size, and (b) measuring in the subject a parameter indicative of the resistance to air flow of the subject's airways.”

Col. 2, lines 35-44. As such, Anderson does not teach or suggest compounds and methods for the treatment of airway diseases and for the delivery of airway drugs as disclosed in the present application.

The Action states that "Boucher, Jr. et al. teach a method for hydrating mucous secretions in lungs, or for treating cystic fibrosis comprising administering to the patient by inhalation benzamil or phenamil . . . ." Action, page 3. However, there is no sufficient motivation to combine Anderson and Boucher, Jr. et al. A person of ordinary skill in the art to which the present invention pertains would not be motivated to combine Anderson (directed to methods and devices for the provocation of airway passage narrowing and/or induction of sputum for diagnostic testing) with Boucher, Jr. et al. (directed to methods of hydrating lung mucous secretions). Such motivation only exists in view of the present invention.

Applicant submits that Jungherr et al. does not supply the missing recitations or motivation to combine these references in order to arrive at the present invention. Instead, Jungherr et al. proposes "[a] sustained release drug delivery composition and a method of making same . . . which comprises microspheres containing a pharmaceutically active agent, a core of a ion-exchange resin and a polymeric coating completely surrounding the core wherein the coating is water-insoluble and hydrolytically stable in physiological environments." Abstract. Although the Action states that "Jungherr et al. teaches that potassium sulfate is known to be biologically compatible with humans and is known to be useful in therapeutic compositions as osmolytes" (Action, page 3), Jungherr et al. does not teach or suggest a method of administering a sodium channel blocker to an airway surface of a subject in need thereof, comprising administering the sodium channel blocker in an effective therapeutic amount in a vehicle, said vehicle comprising potassium sulfate as an ionic osmolyte, said potassium sulfate included in an amount effective to increase the volume of liquid on the airway surface as recited in new Claim 51. Thus, Jungherr et al. does not provide motivation for one of ordinary skill in the art to combine the cited references where one of ordinary skill in the art clearly would not rely on the teachings of Jungherr et al. in pursuit of the present invention.

Applicant submits that even if Anderson, Boucher, Jr. et al., and Jungherr et al. were to be combined, the resultant combination would not be the present invention. The cited references, alone or in combination, fail to provide a method of administering a sodium channel blocker to an airway surface of a subject in need thereof, comprising administering the sodium channel blocker in an effective

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therapeutic amount in a vehicle, said vehicle comprising potassium sulfate as an ionic osmolyte, said potassium sulfate included in an amount effective to increase the volume of liquid on the airway surface as recited in new Claim 51. Moreover, the cited references, as discussed above, lack the recitations that would motivate one of ordinary skill in the art to combine the cited references. Furthermore, the lack of recitations by the cited references do not enable one of ordinary skill in the art to arrive at the present invention as recited in new Claim 51 regardless of requisite motivation to combine references.

Accordingly, Applicant submits that Claims 22-24, 31-32, 37, 44, and 49, and new Claims 51-53 are not obvious in view of Anderson, in view of Boucher, Jr. et al. and Jungherr et al. and requests that this rejection be withdrawn.

### **III. Conclusion**

In view of the foregoing remarks, Applicant respectfully requests that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. Any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,

  
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### **CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on January 16, 2003.

  
Vickie Diane Prior

Date of Signature: January 16, 2003